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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/006,279 | 12/04/2001 | Juan C. Colberg | PC10862A | 2249 |

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[REDACTED] EXAMINER

BERCH, MARK L

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1624

DATE MAILED: 04/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/006,279 | COLBERG ET AL. | |
| | Examiner | Art Unit | |
| | Mark L. Berch | 1624 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 04 March 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-11, 13-16 and 20-24 is/are rejected.
- 7) Claim(s) 12 and 17-19 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____ .
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-11, 13-16, 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/01696.

The acylation process is set forth beginning at page 17, line 24. Note that in the reference, n is required to be zero. Note that CO_2R^3 can be carboxy (or salt thereof), as set forth in e.g. the abstract. In the actual examples, acylation is done with the esters, e.g. examples 1 (step g), 3 (step h), 13 (step g), etc. Thus, the sole difference is that applicants use the acid (or salt), while the reference's specific examples use the esters. But the page 17-18 text teaches that the acid can also be used. Applicants must show unexpected effects arising from the use of the acid rather than the ester. Specifics of solvent, catalyst, etc are present on page 18-22, e.g. page 22, lines 3 and 17 (the carbodiimide coupling agent of claims 14-15 is conventional, and is used in example 22). Hence, claims 1, 5-11, 13-16, 21-22 are obvious

With regard to claim 23-24, example 6 step d; example 7, step a; example 9, step a; example 14, step d; example 15, step d and others all teach the p-methoxybenzyl esters, while the claims have the p-nitrobenzyl ester. However, page 5, lines 14-15 teach this exact equivalence. Clearly, one of ordinary skill in the art would understand that

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either can be used, since both are named on these two lines. By the same reasoning, example 7 renders claim 3 obvious; the claim removes the p-nitrobenzyl group, the example removes the p-methoxybenzyl ester. Likewise, example 1, step h removes the t-butyl group, but again, page 5 teaches that equivalence. See also examples 18-19, 22-23 step b, and many others. Removing either group would be obvious, because page 5 teaches that any of these groups can be used. With regard to claim 4, which has acylation done on a salt, that specific feature is mentioned at page 17, line 26. As for claim 20, these two solvents are listed at page 20, lines 24 and 26.

Claim 2 has deprotecting using a salt starting material. This is seen in example 17, step i; example 1, step h; example 2, step i; example 5, step b; example 12, step h; and others, where the salt is formed first with HCl.

The traverse is unpersuasive. Applicants refer to "unexpected reactivity" as being the unexpected results. Specifically, applicants state that the prior art process requires "high cost cryogenic thermodynamic conditions" whereas their do not. However:

1. Such a difference is not reflected in the actual claim language. That is, no claim sets a lower limit on temperature. Hence, all the claims read on doing the reaction at the same temperatures as are used in the prior art. Patentability cannot be based on limitations not actually present in the claims.
2. The generic discussion of the acylation at pages 17-18 of the reference makes no mention of any temperature requirements. Thus, the reference does not require that low temperatures be used.
3. Applicants have not actually showed that whether the compound is present as a salt/acid versus the ester makes any difference at all in the temperature

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requirements for the reaction. Applicants have simply assumed it without proving it.

It is noted that the specification teaches doing the reaction as low as -40°C (page 3, line 25), and indeed saying nothing about this alleged improvement.

4. It is not true that the examples all have cryogenic conditions either. Example 7(a) does the reaction in "an ice bath", taken to be 0°C. Presumably, the same conditions were used in Example 24e. Likewise, example 12c says that it was done at 0°C, and so it can be assumed that Example 16c was done the same. The same is true for example 17h. Example 30h was done first at 0°C, and then at room temperature. The procedure at example 32g says the "solution was warmed to room temperature over 1 hour"; the same was done in 32h. The reaction at Examples 13g, 27i and 29f give no temperature at all, indicating that it may well have been done at room temperature.

Next, applicants argue that their use of acid/salt "eliminates the need for a costly coupling agent." Again, the claims have no such no-coupling-agent limitation, so the claims read on using a coupling agent which is even recited in the next to last line of claim 1. Second, applicants have not shown that their use of acid/salt does eliminate a need which was there in the first place. Applicants have not even alleged that this is unexpected. Much the same goes for applicants comments about "purging of impurities", "Crystallized without difficulties", etc. There is no evidence for any of this.

In terms of the compound claims 23 and 24, applicants state that "crystalline compounds are of higher purity than the less crystalline compounds." This is purely speculative. Applicants have not shown that their compound is any more pure, or any more crystalline than the compound of the prior art. Applicants next argue that their

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protecting group can be removed with sodium dithionite, and under "mild pH adjustment" whereas the prior art protecting group cannot. This, however, is an expected difference. One of ordinary skill in the art knows that protecting groups require different techniques to remove, including these two. Expected differences cannot overcome obviousness. Incidentally, applicants statement that, "utilization of paramethoxybenzyl requires the use of hydrogenation conditions to remove that group" is untrue. Hydrogenation is the a common method, but such groups have been removed by other methods, such as formic acid, or TFA.

Claims 12 and 17-20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 708-308-1235.



Mark L. Berch
Primary Examiner
Art Unit 1624

April 9, 2003